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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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10/649,413

08/27/2003

Axel Ullrich

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12/11/2007

LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6731

EXAMINER

SHAFFER, SHULAMITH H

ART UNIT

PAPER NUMBER

1647

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--|---------------------------------------|--|
| Office Action Summary | Application No. 10/649,413 | Applicant(s) ULLRICH ET AL. | |
| | Examiner SHULAMITH H. SHAFER | Art Unit 1647 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 September 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,4 and 13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4 and 13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

Status of Application, Amendments, And/Or Claims

The amendment received 21 September 2007 in response to the Office Action of 11 June 2007 has been entered. Claims 1, and 13 have been amended and the amendments have been entered. Claims 1, 3, 4, and 13 are pending and under consideration.

Information Disclosure Statement:

The Information Disclosure statements (IDS) submitted on the 21 September 2007, has been considered. Signed copy is attached.

Withdrawn Rejections

The rejection of Claims 1, 3, 4 and 13 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in part. Applicant's arguments have been found to be persuasive, in part; thus the rejections pertaining to inhibitors wherein the inhibitors are antibodies directed to the FGFR-4 receptor and small molecule RTK inhibitors is withdrawn.

Maintained Rejections 35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claims 1, and 4, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the treatment of a carcinoma in a mammal which method comprises administering to the mammal an effective amount

of at least one inhibitor wherein the inhibitor is a soluble, kinase inactive FGFR-4 does not reasonably provide enablement for a method of administering to the mammal an effective amount of at least one inhibitor wherein the inhibitor is any kinase inactive receptor is maintained for reasons of record in Office Action of 11 June 2007 and for reasons set forth below. Breadth of the claims: The claims recite a method of treatment comprising administration of an effective amount of inhibitor wherein the inhibitor is a kinase-inactive receptor. Given the broadest reasonable interpretation, the claims are directed to administration of any kinase-inactive receptor.

Direction/guidance in the specification: The specification teaches that a kinase-inactive receptor may be used to inhibit the activity of the mutated FGFR-4 receptor [paragraph 0042 of PGPUB 20040067885, the PGPUB of the instant application]. The specification and the art teach that a number of different receptor tyrosine-kinases are overexpressed in certain cancers, such as breast cancers and that inhibition of activity of said receptors by kinase inactive receptors could be used to treat cancers. However, one of ordinary skill in the art could envision only the use of an inactive FGFR-4 kinase receptor in the method of the instant invention. One of ordinary skill in the art would have to undertake undue experimentation to determine which kinase-inactive receptors, other than a kinase-inactive FGFR-4 receptor, could be used in the methods of the instant invention.

Working examples: There are no working or prophetic examples drawn to treatment of any mammal by the methods of the instant invention.

Teachings in the art: Ezzat et al (cited in previous office action of 11 June 2007) teach that truncated FGFRs that lack a tyrosine kinase domain disrupt FGFR signaling; however, there are no teachings in the art as to what other kinase-inactive receptors would function as inhibitors of a mutated FGFR-4 receptors.

Due to the large quantity of experimentation necessary to determine what type of kinase-inactive receptor, other than a truncated, kinase inactive FGFR-4 receptor, would function as an inhibitor of a constitutively active, mutated FGFR-4 receptor, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to same, the breadth of the claims, which are

drawn to treatment with any kinase inactive receptor, the complex nature of the invention, the state of the art which teaches only truncated FGFR-4 receptors as a method of inhibiting FGFR-4 signalling, undue experimentation would be required of the skilled artisan to practice the claimed invention in its full scope.

The rejection of Claims 1, 3, 4 and 13 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record (Office Action of 11 June 2007) and for reasons set forth below.

Applicant traverses the rejection. The reasons for the traversal are that the specification discloses a representative number of species of FGFR-4 inhibitors, such as low molecular weight substances directed against an RTK, a kinase-inactive receptor, and an anti-receptor antibody.

Applicant's arguments have been fully considered and found to be persuasive in part, as directed to a kinase-inactive FGFR-4 receptor and a FGFR-4 anti-receptor antibody. However the rejection is maintained in regard to low molecular weight substances, kinase-inactive receptors other than FGFR-4, or other unspecified substances directed against an RTK.

The claims are directed to a method of treatment comprising administration of at least one inhibitor of the mutated FGFR-4. This is a genus claim, since the inhibitor, as applied to small molecules, encompasses numerous species that are not further described. Applicant asserts that inhibitors were known in the art at the time the subject application was filed (page 4 of response, last paragraph). However, none of the references cited teach a compound that inhibits either the wildtype or the mutated FGFR-4, and thus the art of record does not overcome deficiencies in the specification. In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus: small molecular weight compounds. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Conclusion:

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lorraine Spector/

Primary Examiner, Art Unit 1647

/Shulamith H. Shafer, Ph.D./
Art Unit 1647